```
         1060        1070        1080        1090        1100        1110        1120
           *           *           *           *           *           *           *
ATACCAGGAC ATTGTATGAC GTTCCCTGCT CACATGCCTG CTTTCTTCCT ATAATACAGA TGCTCAACTA

         1130        1140        1150        1160        1170        1180        1190
           *           *           *           *           *           *           *
ACTGCTCATG TCCTTATATC ACAGAGGGAA ATTGGAGCTA TCTGAGGAAC TGCCCAGAAG GGAAGGGCAG

         1200        1210        1220        1230        1240        1250        1260
           *           *           *           *           *           *           *
AGGGGTCTTG CTCTCCTTGT CTGAGCCATA ACTCTTCTTT CTACCTTCCA GTGAACACCT TCCCACCCCA

         1270        1280        1290        1300        1310        1320        1330
           *           *           *           *           *           *           *
GGTCCACCTG CTACCGCCGC CGTCGGAGGA GCTGGCCCTG AATGAGCTCT TGTCCCTGAC ATGCCTGGTG

         1340        1350        1360        1370        1380        1390        1400
           *           *           *           *           *           *           *
CGAGCTTTCA ACCCTAAAGA AGTGCTGGTG CGATGGCTGC ATGGAAATGA GGAGCTGTCC CCAGAAAGCT

         1410        1420        1430        1440        1450        1460        1470
           *           *           *           *           *           *           *
ACCTAGTGTT TGAGCCCCTA AAGGAGCCAG GCGAGGGAGC CACCACCTAC CTGGTGACAA GGGTGTTGCG

         1480        1490        1500        1510        1520        1530        1540
           *           *           *           *           *           *           *
TGTATCAGCT GAAAGCTTGA TATCGAATTC CGGAGGCGGA ACCGGCAGTG CAGCCCGAAG CCCCGCAGTC

         1550        1560        1570        1580        1590
           *           *           *           *           *           *
CCCGAGCACG CGTGGCC ATG CGT CCC CTG CGC CCC CGC GCC GCG CTG CTG GCG CTC CTG
                    Met Arg Pro Leu Arg Pro Arg Ala Ala Leu Leu Ala Leu Leu>
                    ___a___a___a___a___a__ORF RF[1] ___a___a___a___a___a___>

  1600        1610        1620        1630        1640        1650
    *           *           *           *           *           *           *
GCC TCG CTC CTG GCC GCG CCC CCG GTG GCC CCG GCC GAG GCC CCG CAC CTG GTG CAT
Ala Ser Leu Leu Ala Ala Pro Pro Val Ala Pro Ala Glu Ala Pro His Leu Val His>
___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

  1660        1670        1680        1690        1700        1710
    *           *           *           *           *           *
GTG GAC GCG GCC CGC GCG CTG TGG CCC CTG CGG CGC TTC TGG AGG AGC ACA GGC TTC
Val Asp Ala Ala Arg Ala Leu Trp Pro Leu Arg Arg Phe Trp Arg Ser Thr Gly Phe>
___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

    1720        1730        1740        1750        1760        1770
      *           *           *           *           *           *           *
TGC CCC CCG CTG CCA CAC AGC CAG GCT GAC CAG TAC GTC CTC AGC TGG GAC CAG CAG
Cys Pro Pro Leu Pro His Ser Gln Ala Asp Gln Tyr Val Leu Ser Trp Asp Gln Gln>
___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

      1780        1790        1900        1810        1820
        *           *           *           *           *           *           *
CTC AAC CTC GCC TAT GTG GGC GCC GTC CCT CAC CGC GGC ATC AAG CAG GTC CGG ACC
Leu Asn Leu Ala Tyr Val Gly Ala Val Pro His Arg Gly Ile Lys Gln Val Arg Thr>
___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

  1830        1840        1850        1860        1870        1880
    *           *           *           *           *           *
CAC TGG CTG CTG GAG CTT GTC ACC ACC AGG GGG TCC ACT GGA CGG GGC CTG AGC TAC
His Trp Leu Leu Glu Leu Val Thr Thr Arg Gly Ser Thr Gly Arg Gly Leu Ser Tyr>
```

## FIGURE 1A

```
             1890        1900        1910        1920        1930        1940
      *       *       *       *       *       *       *       *       *       *       *       *
     AAC TTC ACC CAC CTG GAC GGG TAC CTG GAC CTT CTC AGG GAG AAC CAG CTC CTC CCA
     Asn Phe Thr His Leu Asp Gly Tyr Leu Asp Leu Leu Arg Glu Asn Gln Leu Leu Pro>
```

```
                 1950        1960        1970        1980        1990
          *       *       *       *       *       *       *       *       *       *       *
     GGG TTT GAG CTG ATG GGC AGC GCC TCG GGC CAC TTC ACT GAC TTT GAG GAC AAG CAG
     Gly Phe Glu Leu Met Gly Ser Ala Ser Gly His Phe Thr Asp Phe Glu Asp Lys Gln>
```

```
     2000        2010        2020        2030        2040        2050
      *       *       *       *       *       *       *       *       *       *       *       *
     CAG GTG TTT GAG TGG AAG GAC TTG GTC TCC AGC CTG GCC AGG AGA TAC ATC GGT AGG
     Gln Val Phe Glu Trp Lys Asp Leu Val Ser Ser Leu Ala Arg Arg Tyr Ile Gly Arg>
```

```
         2060        2070        2080        2090        2100        2110
          *       *       *       *       *       *       *       *       *       *       *
     TAC GGA CTG GCG CAT GTT TCC AAG TGG AAC TTC GAG ACG TGG AAT GAG CCA GAC CAC
     Tyr Gly Leu Ala His Val Ser Lys Trp Asn Phe Glu Thr Trp Asn Glu Pro Asp His>
```

```
            2120        2130        2140        2150        2160
          *       *       *       *       *       *       *       *       *       *       *
     CAC GAC TTT GAC AAC GTC TCC ATG ACC ATG CAA GGC TTC CTG AAC TAC TAC GAT GCC
     His Asp Phe Asp Asn Val Ser Met Thr Met Gln Gly Phe Leu Asn Tyr Tyr Asp Ala>
```

```
     2170        2180        2190        2200        2210        2220
      *       *       *       *       *       *       *       *       *       *       *       *
     TGC TCG GAG GGT CTG CGC GCC GCC AGC CCC GCC CTG CGG CTG GGA GGC CCC GGC GAC
     Cys Ser Glu Gly Leu Arg Ala Ala Ser Pro Ala Leu Arg Leu Gly Gly Pro Gly Asp>
```

```
       2230        2240        2250        2260        2270        2280
          *       *       *       *       *       *       *       *       *       *       *
     TCC TTC CAC ACC CCA CCG CGA TCC CCG CTG AGC TGG GGC CTC CTG CGC CAC TGC CAC
     Ser Phe His Thr Pro Pro Arg Ser Pro Leu Ser Trp Gly Leu Leu Arg His Cys His>
```

```
          2290        2300        2310        2320        2330        2340
          *       *       *       *       *       *       *       *       *       *       *
     GAC GGT ACC AAC TTC TTC ACT GGG GAG GCG GGC GTG CGG CTG GAC TAC ATC TCC CTC
     Asp Gly Thr Asn Phe Phe Thr Gly Glu Ala Gly Val Arg Leu Asp Tyr Ile Ser Leu>
```

```
          2350        2360        2370        2380        2390
          *       *       *       *       *       *       *       *       *       *
     CAC AGG AAG GGT GCG CGC AGC TCC ATC TCC ATC CTG GAG CAG GAG AAG GTC GTC GCG
     His Arg Lys Gly Ala Arg Ser Ser Ile Ser Ile Leu Glu Gln Glu Lys Val Val Ala>
```

```
     2400        2410        2420        2430        2440        2450
      *       *       *       *       *       *       *       *       *       *       *
     CAG CAG ATC CGG CAG CTC TTC CCC AAG TTC GCG GAC ACC CCC ATT TAC AAC GAC GAG
     Gln Gln Ile Arg Gln Leu Phe Pro Lys Phe Ala Asp Thr Pro Ile Tyr Asn Asp Glu>
```

## FIGURE 1B

```
        2460              2470              2480              2490              2500              2510
     *       *       *       *       *       *       *       *       *       *       *       *
     GCG GAC CCG CTG GTG GGC TGG TCC CTG CCA CAG CCG TGG AGG GCG GAC GTG ACC TAC
     Ala Asp Pro Leu Val Gly Trp Ser Leu Pro Gln Pro Trp Arg Ala Asp Val Thr Tyr>
     ___a___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

            2520              2530              2540              2550              2560
        *       *       *       *       *       *       *       *       *       *
     GCG GCC ATG GTG GTG AAG GTC ATC GCG CAG CAT CAG AAC CTG CTA CTG GCC AAC ACC
     Ala Ala Met Val Val Lys Val Ile Ala Gln His Gln Asn Leu Leu Leu Ala Asn Thr>
     ___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

   2570          2580              2590              2600              2610              2620
     *       *       *       *       *       *       *       *       *       *       *
     ACC TCC GCC TTC CCC TAC GCG CTC CTG AGC AAC GAC AAT GCC TTC CTG AGC TAC CAC
     Thr Ser Ala Phe Pro Tyr Ala Leu Leu Ser Asn Asp Asn Ala Phe Leu Ser Tyr His>
     ___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

        2630              2640              2650              2660              2670              2680
        *       *       *       *       *       *       *       *       *       *
     CCG CAC CCC TTC GCG CAG CGC ACG CTC ACC GCG CGC TTC CAG GTC AAC AAC ACC CGC
     Pro His Pro Phe Ala Gln Arg Thr Leu Thr Ala Arg Phe Gln Val Asn Asn Thr Arg>
     ___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

            2690              2700              2710              2720              2730
        *       *       *       *       *       *       *       *       *       *
     CCG CCG CAC GTG CAG CTG TTG CGC AAG CCG GTG CTC ACG GCC ATG GGG CTG CTG GCG
     Pro Pro His Val Gln Leu Leu Arg Lys Pro Val Leu Thr Ala Met Gly Leu Leu Ala>
     ___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

   2740          2750              2760              2770              2780              2790
     *       *       *       *       *       *       *       *       *       *       *
     CTG CTG GAT GAG GAG CAG CTC TGG GCC GAA GTG TCG CAG GCC GGG ACC GTC CTG GAC
     Leu Leu Asp Glu Glu Gln Leu Trp Ala Glu Val Ser Gln Ala Gly Thr Val Leu Asp>
     ___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

   2800          2810              2820              2830              2840              2850
     *       *       *       *       *       *       *       *       *       *       *
     AGC AAC CAC ACG GTG GGC GTC CTG GCC AGC GCC CAC CGC CCC CAG GGC CCG GCC GAC
     Ser Asn His Thr Val Gly Val Leu Ala Ser Ala His Arg Pro Gln Gly Pro Ala Asp>
     ___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

        2860              2870              2880              2890              2900              2910
        *       *       *       *       *       *       *       *       *       *
     GCC TGG CGC GCC GCG GTG CTG ATC TAC GCG AGC GAC GAC ACC CGC GCC CAC CCC AAC
     Ala Trp Arg Ala Ala Val Leu Ile Tyr Ala Ser Asp Asp Thr Arg Ala His Pro Asn>
     ___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

            2920              2930              2940              2950              2960
        *       *       *       *       *       *       *       *       *       *
     CGC AGC GTC GCG GTG ACC CTG CGG CTG CGC GGG GTG CCC CCC GGC CCG GGC CTG GTC
     Arg Ser Val Ala Val Thr Leu Arg Leu Arg Gly Val Pro Pro Gly Pro Gly Leu Val>
     ___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

   2970          2980              2990              3000              3010              3020
     *       *       *       *       *       *       *       *       *       *       *
     TAC GTC ACG CGC TAC CTG GAC AAC GGG CTC TGC AGC CCC GAC GGC GAG TGG CGG CGC
     Tyr Val Thr Arg Tyr Leu Asp Asn Gly Leu Cys Ser Pro Asp Gly Glu Trp Arg Arg>
     ___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

        3030              3040              3050              3060              3070              3080
        *       *       *       *       *       *       *       *       *       *
```

**FIGURE 1C**

```
CTG GGC CGG CCC GTC TTC CCC ACG GCA GAG CAG TTC CGG CGC ATG CGC GCG GCT GAG
Leu Gly Arg Pro Val Phe Pro Thr Ala Glu Gln Phe Arg Arg Met Arg Ala Ala Glu>
___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

            3090         3100         3110         3120         3130
             *            *     *      *     *      *     *      *     *
GAC CCG GTG GCC GCG GCG CCC CGC CCC TTA CCC GCC GGC GGC CGC CTG ACC CTG CGC
Asp Pro Val Ala Ala Ala Pro Arg Pro Leu Pro Ala Gly Gly Arg Leu Thr Leu Arg>
___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

3140         3150         3160         3170         3180         3190
  *     *      *     *      *     *      *     *      *     *      *     *
CCC GCG CTG CGG CTG CCG TCG CTT TTG CTG GTG CAC GTG TGT GCG CGC CCC GAG AAG
Pro Ala Leu Arg Leu Pro Ser Leu Leu Leu Val His Val Cys Ala Arg Pro Glu Lys>
___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

   3200         3210         3220         3230         3240         3250
    *     *      *     *      *     *      *     *      *     *      *     *
CCG CCC GGG CAG GTC ACG CGG CTC CGC GCC CTG CCC CTG ACC CAA GGG CAG CTG GTT
Pro Pro Gly Gln Val Thr Arg Leu Arg Ala Leu Pro Leu Thr Gln Gly Gln Leu Val>
___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

       3260         3270         3280         3290         3300
    *      *     *      *     *      *     *      *     *      *     *
CTG GTC TGG TCG GAT GAA CAC GTG GGC TCC AAG TGC CTG TGG ACA TAC GAG ATC CAG
Leu Val Trp Ser Asp Glu His Val Gly Ser Lys Cys Leu Trp Thr Tyr Glu Ile Gln>
___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

3310         3320         3330         3340         3350         3360
  *     *      *     *      *     *      *     *      *     *      *     *
TTC TCT CAG GAC GGT AAG GCG TAC ACC CCG GTC AGC AGG AAG CCA TCG ACC TTC AAC
Phe Ser Gln Asp Gly Lys Ala Tyr Thr Pro Val Ser Arg Lys Pro Ser Thr Phe Asn>
___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

  3370         3380         3390         3400         3410         3420
   *     *      *     *      *      *     *      *     *      *     *
CTC TTT GTG TTC AGC CCA GAC ACA GGT GCT GTC TCT GGC TCC TAC CGA GTT CGA GCC
Leu Phe Val Phe Ser Pro Asp Thr Gly Ala Val Ser Gly Ser Tyr Arg Val Arg Ala>
___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

       3430         3440         3450         3460         3470         3480
    *      *  -   *      *      *     *      *     *      *     *      *     *
CTG GAC TAC TGG GCC CGA CCA GGC CCC TTC TCG GAC CCT GTG CCG TAC CTG GAG GTC
Leu Asp Tyr Trp Ala Arg Pro Gly Pro Phe Ser Asp Pro Val Pro Tyr Leu Glu Val>
___a___a___a___a___a___a___a____ORF RF[1] _a___a___a___a___a___a___a___a___>

          3490         3500         3510         3520         3530         3540
    *      *     *      *      *     *      *     *      *     *      *
CCT GTG CCA AGA GGG CCC CCA TCC CCG GGC AAT CCA TGAG CCTGTGCTGA GCCCCAGTGG
Pro Val Pro Arg Gly Pro Pro Ser Pro Gly Asn Pro>
___a___a___a___a_ORF RF[1] ___a___a___a___a___>

       3550         3560         3570         3580         3590         3600         3610
        *     *      *     *      *      *     *      *     *      *     *      *
GTTGCACCTC CACCGGCAGT CAGCGAGCTG GGGCTGCACT GTGCCCATGC TGCCCTCCCA TCACCCCCTT

       3620         3630         3640         3650         3660         3670         3680
        *     *      *     *      *      *     *      *     *      *     *      *
TGCAATATAT TTTTATATTT TAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA

       3690         3700         3710         3720         3730         3740         3750
        *     *      *     *      *      *     *      *     *      *     *
```

FIGURE 1D

```
AAAAAAAAAA AAAAAAAAAG AATTCCTGCA GCCCGGGGGA TCCACTAGTT CTAGAGGGCC CGTTTAAACC

     3760       3770       3780       3790       3800       3810       3820
      *          *          *          *          *          *          *
CGCTGATCAG CCTCGACTGT GCCTTCTAGT TGCCAGCCAT CTGTTGTTTG CCCCTCCCCC GTGCCTTCCT

     3830       3840       3850       3860       3870       3880       3890
      *          *          *          *          *          *          *
TGACCCTGGA AGGTGCCACT CCCACTGTCC TTTCCTAATA AAATGAGGAA ATTGCATCGC ATTGTCTGAG

     3900       3910       3920       3930       3940       3950       3960
      *          *          *          *          *          *          *
TAGGTGTCAT TCTATTCTGG GGGGTGGGGT GGGGCAGGAC AGCAAGGGGG AGGATTGGGA AGACAATAGC

     3970       3980       3990       4000       4010       4020       4030
      *          *          *          *          *          *          *
AGGCATGCTG GGGATGCGGT GGGCTCTATG GCTTCTGAGG CGGAAAGAAC CAGCTGGGGC TCGAGAGCTT

     4040       4050       4060       4070       4080       4090       4100
      *          *          *          *          *          *          *
GGCGTAATCA TGGTCATAGC TGTTTCCTGT GTGAAATTGT TATCCGCTCA CAATTCCACA CAACATACGA

     4110       4120       4130       4140       4150       4160       4170
      *          *          *          *          *          *          *
GCCGGAAGCA TAAAGTGTAA AGCCTGGGGT GCCTAATGAG TGAGCTAACT CACATTAATT GCGTTGCGCT

     4180       4190       4200       4210       4220       4230       4240
      *          *          *          *          *          *          *
CACTGCCCGC TTTCCAGTCG GGAAACCTGT CGTGCCAGCT GCATTAATGA ATCGGCCAAC GCGCGGGGAG

     4250       4260       4270       4280       4290       4300       4310
      *          *          *          *          *          *          *
AGGCGGTTTG CGTATTGGGC GCTCTTCCGC TTCCTCGCTC ACTGACTCGC TGCGCTCGGT CGTTCGGCTG

     4320       4330       4340       4350       4360       4370       4380
      *          *          *          *          *          *          *
CGGCGAGCGG TATCAGCTCA CTCAAAGGCG GTAATACGGT TATCCACAGA ATCAGGGGAT AACGCAGGAA

     4390       4400       4410       4420       4430       4440       4450
      *          *          *          *          *          *          *
AGAACATGTG AGCAAAAGGC CAGCAAAAGG CCAGGAACCG TAAAAAGGCC GCGTTGCTGG CGTTTTTCCA

     4460       4470       4480       4490       4500       4510       4520
      *          *          *          *          *          *          *
TAGGCTCCGC CCCCCTGACG AGCATCACAA AAATCGACGC TCAAGTCAGA GGTGGCGAAA CCCGACAGGA

     4530       4540       4550       4560       4570       4580       4590
      *          *          *          *          *          *          *
CTATAAAGAT ACCAGGCGTT TCCCCCTGGA AGCTCCCTCG TGCGCTCTCC TGTTCCGACC CTGCCGCTTA

     4600       4610       4620       4630       4640       4650       4660
      *          *          *          *          *          *          *
CCGGATACCT GTCCGCCTTT CTCCCTTCGG GAAGCGTGGC GCTTTCTCAA TGCTCACGCT GTAGGTATCT

     4670       4680       4690       4700       4710       4720       4730
      *          *          *          *          *          *          *
CAGTTCGGTG TAGGTCGTTC GCTCCAAGCT GGGCTGTGTG CACGAACCCC CCGTTCAGCC CGACCGCTGC

     4740       4750       4760       4770       4780       4790       4800
      *          *          *          *          *          *          *
GCCTTATCCG GTAACTATCG TCTTGAGTCC AACCCGGTAA GACACGACTT ATCGCCACTG GCAGCAGCCA
```

**FIGURE 1E**

```
        4810          4820          4830          4840          4850          4860          4870
          *             *             *             *             *             *             *
CTGGTAACAG GATTAGCAGA GCGAGGTATG TAGGCGGTGC TACAGAGTTC TTGAAGTGGT GGCCTAACTA

        4880          4890          4900          4910          4920          4930          4940
          *             *             *             *             *             *             *
CGGCTACACT AGAAGGACAG TATTTGGTAT CTGCGCTCTG CTGAAGCCAG TTACCTTCGG AAAAAGAGTT

        4950          4960          4970          4980          4990          5000          5010
          *             *             *             *             *             *             *
GGTAGCTCTT GATCCGGCAA ACAAACCACC GCTGGTAGCG GTGGTTTTTT TGTTTGCAAG CAGCAGATTA

        5020          5030          5040          5050          5060          5070          5080
          *             *             *             *             *             *             *
CGCGCAGAAA AAAAGGATCT CAAGAAGATC CTTTGATCTT TTCTACGGGG TCTGACGCTC AGTGGAACGA

        5090          5100          5110          5120          5130          5140          5150
          *             *             *             *             *             *             *
AAACTCACGT TAAGGGATTT TGGTCATGAG ATTATCAAAA AGGATCTTCA CCTAGATCCT TTTAAATTAA

        5160          5170          5180          5190          5200          5210          5220
          *             *             *             *             *             *             *
AAATGAAGTT TTAAATCAAT CTAAAGTATA TATGAGTAAA CTTGGTCTGA CAGTTACCAA TGCTTAATCA

        5230          5240          5250          5260          5270          5280          5290
          *             *             *             *             *             *             *
GTGAGGCACC TATCTCAGCG ATCTGTCTAT TTCGTTCATC CATAGTTGCC TGACTCCCCG TCGTGTAGAT

        5300          5310          5320          5330          5340          5350          5360
          *             *             *             *             *             *             *
AACTACGATA CGGGAGGGCT TACCATCTGG CCCCAGTGCT GCAATGATAC CGCGAGACCC ACGCTCACCG

        5370          5380          5390          5400          5410          5420          5430
          *             *             *             *             *             *             *
GCTCCAGATT TATCAGCAAT AAACCAGCCA GCCGGAAGGG CCGAGCGCAG AAGTGGTCCT GCAACTTTAT

        5440          5450          5460          5470          5480          5490          5500
          *             *             *             *             *             *             *
CCGCCTCCAT CCAGTCTATT AATTGTTGCC GGGAAGCTAG AGTAAGTAGT TCGCCAGTTA ATAGTTTGCG

        5510          5520          5530          5540          5550          5560          5570
          *             *             *             *             *             *             *
CAACGTTGTT GCCATTGCTA CAGGCATCGT GGTGTCACGC TCGTCGTTTG GTATGGCTTC ATTCAGCTCC

        5580          5590          5600          5610          5620          5630          5640
          *             *             *             *             *             *             *
GGTTCCCAAC GATCAAGGCG AGTTACATGA TCCCCCATGT TGTGCAAAAA AGCGGTTAGC TCCTTCGGTC

        5650          5660          5670          5680          5690          5700          5710
          *             *             *             *             *             *             *
CTCCGATCGT TGTCAGAAGT AAGTTGGCCG CAGTGTTATC ACTCATGGTT ATGGCAGCAC TGCATAATTC

        5720          5730          5740          5750          5760          5770          5780
          *             *             *             *             *             *             *
TCTTACTGTC ATGCCATCCG TAAGATGCTT TTCTGTGACT GGTGAGTACT CAACCAAGTC ATTCTGAGAA

        5790          5800          5810          5820          5830          5840          5850
          *             *             *             *             *             *             *
TAGTGTATGC GGCGACCGAG TTGCTCTTGC CCGGCGTCAA TACGGGATAA TACCGCGCCA CATAGCAGAA

        5860          5870          5880          5890          5900          5910          5920
          *             *             *             *             *             *             *
```

## FIGURE 1F
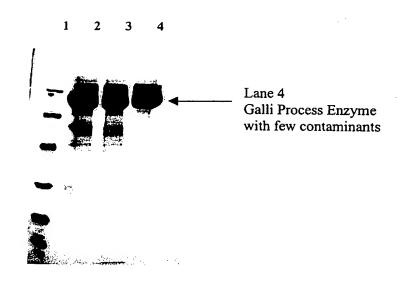
CTTTAAAAGT GCTCATCATT GGAAAACGTT CTTCGGGGCG AAAACTCTCA AGGATCTTAC CGCTGTTGAG

   5930      5940      5950      5960      5970      5980      5990
  *     *    *    *    *    *    *    *    *    *    *    *    *
ATCCAGTTCG ATGTAACCCA CTCGTGCACC CAACTGATCT TCAGCATCTT TTACTTTCAC CAGCGTTTCT

   6000      6010      6020      6030      6040      6050      6060
  *     *    *    *    *    *    *    *    *    *    *    *    *
GGGTGAGCAA AAACAGGAAG GCAAAATGCC GCAAAAAAGG GAATAAGGGC GACACGGAAA TGTTGAATAC

   6070      6080      6090      6100      6110      6120      6130
  *     *    *    *    *    *    *    *    *    *    *    *    *
TCATACTCTT CCTTTTTCAA TATTATTGAA GCATTTATCA GGGTTATTGT CTCATGAGCG GATACATATT

   6140      6150      6160      6170      6180      6190      6200
  *     *    *    *    *    *    *    *    *    *    *    *    *
TGAATGTATT TAGAAAAATA AACAAATAGG GGTTCCGCGC ACATTCCCC GAAAAGTGCC ACCTGACGTC

FIGURE 1G

## FIGURE 2. SDS-POLYACRYLAMIDE GELS DEMONSTRATING IMPROVEMENTS IN PURITY

Gel using the Kakkis et al 1994, published procedure for purification



— Contaminant

Iduronidase  3 ug

Contaminants

Gel using the new Galli Process contained in this application



1    2    3    4

Lane 4
Galli Process Enzyme
with few contaminants

1.  Molecular Weight Marker
2.  Prior Process Carson (nonpublished)  Batch  2000C9001 Reference Reduced (7.5 µg)
3.  Same Batch  2000C9001 Reference Reduced (5.0 µg)
4.  Galli Process Enzyme Batch P10006 (5.0 µg)

# FIGURE 2

**FIGURE 3A  IDURONIDASE PRODUCTION USING THE GALLI PROCESS**
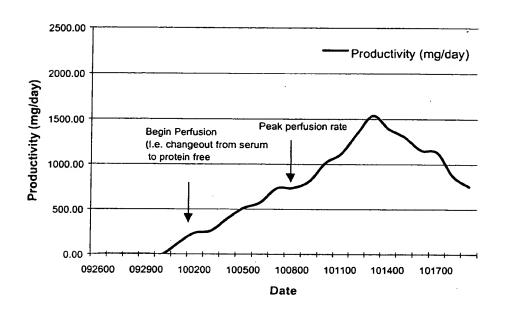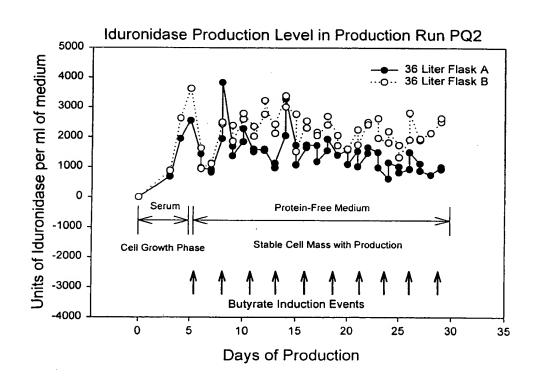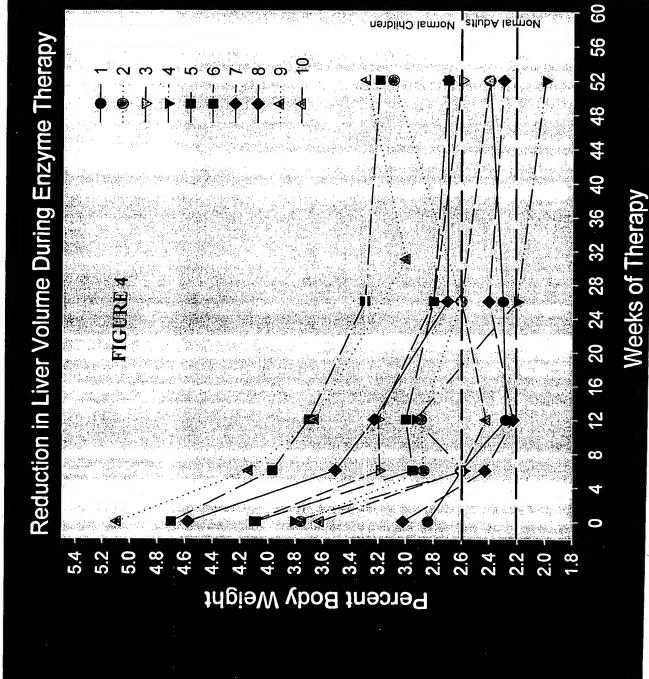
**Iduronidase Enzyme Activity During Production**



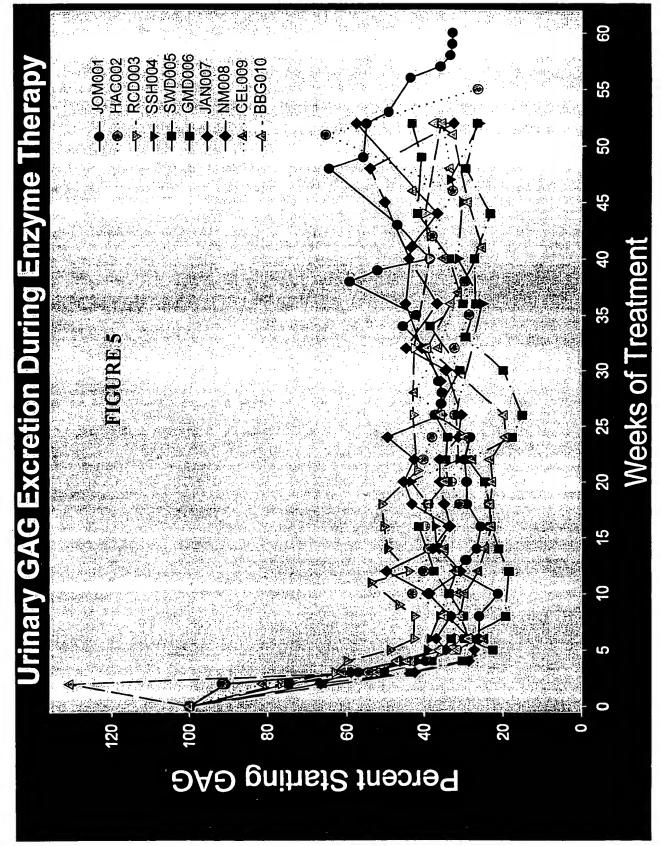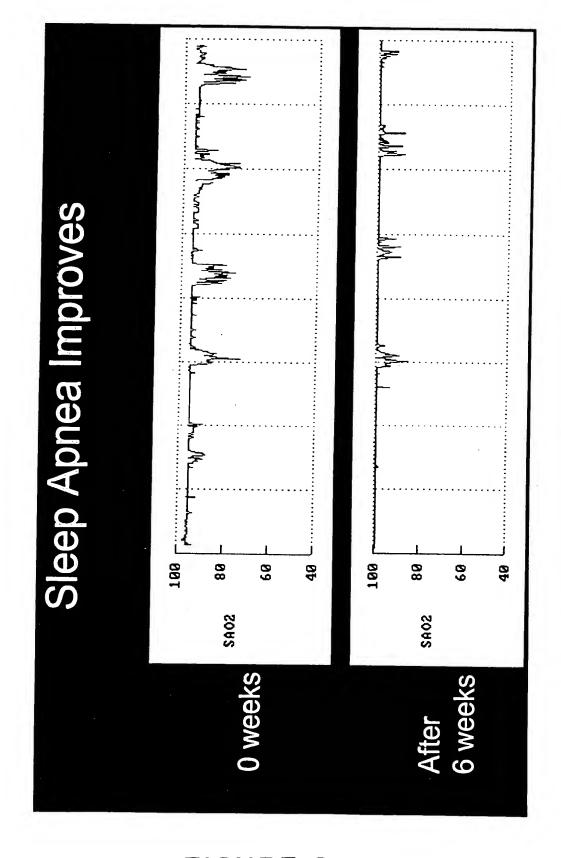**FIGURE 3B.  IDURONIDASE PRODUCTION USING BUTYRATE INDUCTION**

Reduction in Liver Volume During Enzyme Therapy

FIGURE 4

FIGURE 4

**Urinary GAG Excretion During Enzyme Therapy**

FIGURE 5

Legend:
- JOM001
- HAC002
- RCD003
- SSH004
- SWD005
- GMD006
- JAN007
- NM008
- CEL009
- BBG010

X-axis: Weeks of Treatment

Y-axis: Percent Starting GAG

FIGURE 5

Elbow and Knee Extension in HAC002



Legend:
- Right Elbow
- Left Elbow
- Right Knee
- Left Knee

Y-axis: Degrees (135, 140, 145, 150, 155, 160, 165, 170, 175, 180)

X-axis: Weeks (0, 10, 20, 30, 40, 50, 60)

FIGURE 6

Shoulder flexion to 104 weeks in four patients with most restriction

FIGURE 7

Sleep Apnea Improves

FIGURE 8

**FIGURE 9**

Pulmonary Function Tests in GMD006

52 wks

230% Improvement

12

0

FVC   FEV1   FEV3

1.6  1.4  1.2  1  0.8  0.6  0.4  0.2  0

FIGURE 10

Increased Height Growth Velocity

FIGURE 11
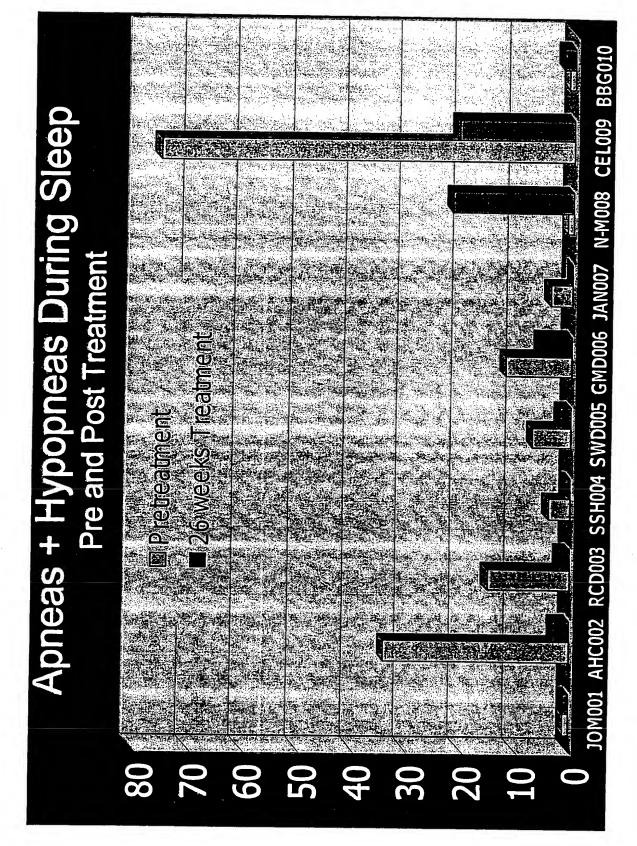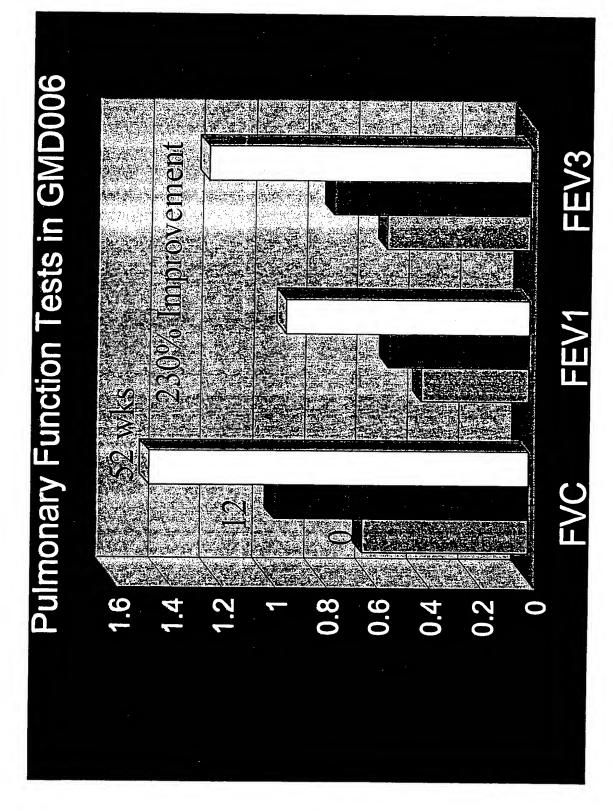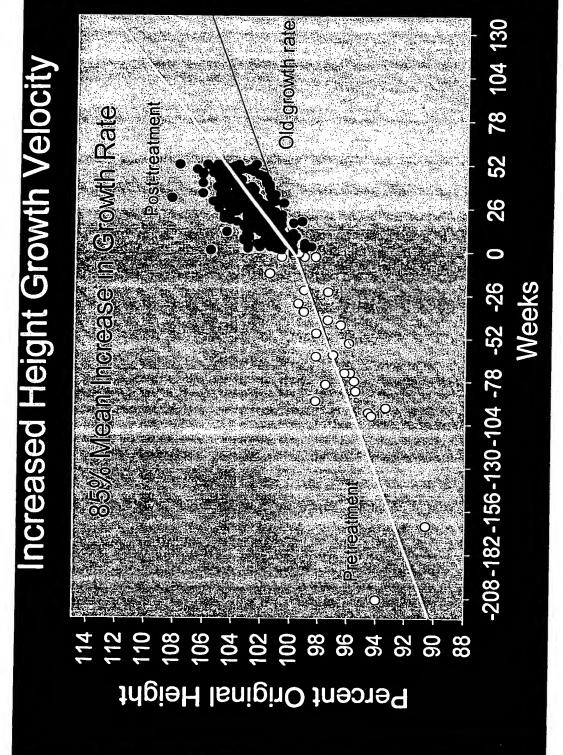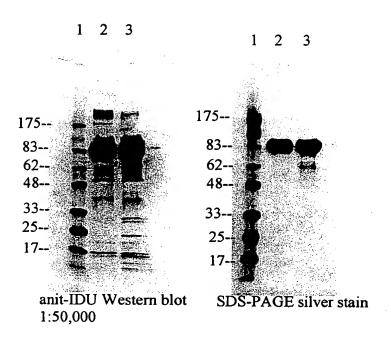
# FIGURE 12.

## COMPARISON OF HOST PROTEIN CONTAMINATION BETWEEN A PRIOR AND THE NEW GALLI PROCESS

Chinese Hamster Ovary Host Protein Contamination by ELISA Assay

| SOURCE AND BATCH NUMBER | CHOP PROTEIN CONTAMINATION (microgram per milligram) | PERCENT CHOP CONTAMINATION | PURITY OF THE ENZYME FROM CHOP |
|---|---|---|---|
| Prior Process (Carson/REI) | | | |
| C9002 | 14 | 1.4% | 98.6% |
| C9003 | 24 | 2.4% | 97.6% |
| C9004 | 16 | 1.6% | 98.4% |
| New Process (Galli) | | | |
| P1003 | <1.3 | <0.13% | >99.9% |
| P1006 | 1.2 | 0.12% | 99.9% |
| P1007 | <0.6 | <0.06% | >99.9% |
| P1008 | <0.67 | <0.067% | >99.9% |

FIGURE 12

# Comparison of Galli and Carson Material



anit-IDU Western blot
1:50,000

SDS-PAGE silver stain

1 Marker
2 Galli Referenced-0201
3 Carson C9002

5ug/lane

# FIGURE 13